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## Estimation of exposure to atmospheric pollutants during pregnancy integrating space-time activity and indoor air levels: does it make a difference?

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### Abstract

Studies of air pollution effects during pregnancy generally only consider exposure in the outdoor air at the home address. We aimed to compare exposure models differing in their ability to account for the spatial resolution of pollutants, space-time activity and indoor air pollution levels. We recruited 40 pregnant women in the Grenoble urban area, France, who carried a Global Positioning System (GPS) during up to 3 weeks; in a subgroup, indoor measurements of fine particles (PM<sub>2.5</sub>) were conducted at home (n=9) and personal exposure to nitrogen dioxide (NO<sub>2</sub>) was assessed using passive air samplers (n=10). Outdoor concentrations of NO<sub>2</sub> and PM<sub>2.5</sub> were estimated from a dispersion model with a fine spatial resolution. Women spent on average 16 h per day at home. Considering only outdoor levels, for estimates at the home address, the correlation between the estimate using the nearest background air monitoring station and the estimate from the dispersion model was high (r=0.93) for PM<sub>2.5</sub> and moderate (r=0.67) for NO<sub>2</sub>. The model incorporating clean GPS data was less correlated with the estimate relying on raw GPS data (r=0.77) than the model ignoring space-time activity (r=0.93). PM<sub>2.5</sub> outdoor levels were not to moderately correlated with estimates from the model incorporating indoor measurements and space-time activity (r=-0.10 to 0.47), while NO<sub>2</sub> personal levels were not correlated with outdoor levels (r=-0.42 to 0.03). In this urban area, accounting for space-time activity little influenced exposure estimates; in a subgroup of subjects (n=9), incorporating indoor pollution levels seemed to strongly modify them.

### Keywords

Exposure assessment; Air pollutants; Space-time activity; Global Positioning System; Indoor environment; Pregnancy

## INTRODUCTION

Epidemiological studies have suggested adverse effects of outdoor air pollution during pregnancy on maternal and fetal health events such as pre-eclampsia, preterm birth, low birth weight, cardiac congenital malformations and intra-uterine growth retardation (Madsen et al., 2010; Pedersen et al., 2014, 2013; Salam et al., 2005; Shah and Balkhair, 2011; Slama et al., 2007a, 2007b; Vrijheid et al., 2011). This literature has some limitations, in particular in terms of exposure assessment.

Various approaches have been used to estimate exposure to atmospheric pollutants in these epidemiological studies. Many studies used air quality monitoring stations to assign exposure levels to large population, using data from the monitoring station closest to the subject's home address (Ritz and Yu, 1999). More recently, land-use regression (LUR) (Nethery et al., 2008b; Pedersen et al., 2013; Sellier et al., 2014; Slama et al., 2007a) and dispersion models (Wu et al., 2009) have been applied.

Improving the spatial resolution of exposure models may be of limited relevance if no effort is made to assess accurately where study subjects spend their time. However, so far, a person's activity throughout the day has rarely been taken into account in the exposure models used in epidemiological publications (Aguilera et al., 2009; de Nazelle et al., 2013; Nethery et al., 2014; Slama et al., 2008). Space-time activity data can be collected by interviews, diaries, as well as Global Positioning System (GPS) tracking data (Wu et al., 2010). Activity diaries are easy to implement but may suffer from recall errors, they require cumbersome post-processing by the research team (e.g., to geocode data) and do not easily allow considering exposures during commuting. GPS devices can now also be used. Advantages of using GPS devices include light weight, small size, non-obtrusive and continuous measurements (Schutz and Chambaz, 1997); the potential limitations include geolocalization errors and the fact that GPS devices often fail to record position indoors (particularly in concrete buildings) and in dense urban areas (Gerharz et al., 2013; Maddison and Ni Mhurchu, 2009), resulting in the need for a data cleaning step. GPS devices and diaries should not be opposed, but can be used simultaneously to complement each other. Personal exposures are also greatly influenced by levels of air pollutant in indoor environments, where people from industrialized countries spend about 80% of their time (Gauvin et al., 2002; Nethery et al., 2008a). In a study of pregnant women conducted in Sabadell, Spain, personal NO<sub>2</sub> levels were more influenced by indoor than by outdoor NO<sub>2</sub> levels (Valero et al., 2009). For 24-hour measurement periods in the general population, correlations between indoor and outdoor fine particles (PM<sub>2.5</sub>) concentrations of 0.80 and 0.68 were reported in Amsterdam and Helsinki, respectively (Brunekreef et al., 2005), while correlations of 0.63 were reported between indoor and outdoor PM<sub>2.5</sub> concentrations for 2-day measurements and of 0.53 for nitrogen dioxide (NO<sub>2</sub>) concentrations for 7-day measurements among pregnant women in Barcelona (Schembari et al., 2013). Correlations may be different according to the study area, ventilation rate, and to whether one considers short or long time periods of exposure, as the contribution of temporal variations to the overall variability in exposure is smaller when longer time periods are considered.

Poor spatial resolution of environmental models, lack of consideration of space-time activity and of indoor air levels might have a strong impact in terms of exposure misclassification. However the relative contribution of these parameters to exposure misclassification has little been assessed (Brunekreef et al., 2005; Dias and Tchepel, 2014; Nethery et al., 2008b; Schembari et al., 2013). Studies simultaneously using several exposure models have demonstrated that the amplitude of the measurement error may be large (Avery et al., 2010; Lepeule et al., 2010; Nethery et al., 2008b; Sellier et al., 2014). Exposure misclassification can strongly bias estimated dose-response functions (depending on its nature) and impact statistical power (de Klerk et al., 1989).

Our objective was to compare different approaches allowing to characterize exposure to PM<sub>2.5</sub> and NO<sub>2</sub> among pregnant women. More specifically, we compared air pollutant exposures assessed by various exposure models that differed by their ability to take into account the spatial variations of the pollutants concentrations, subjects' space-time activity and PM<sub>2.5</sub> indoor air levels. A secondary aim was to illustrate the impact on the estimated exposures of cleaning the GPS data used to characterize space-time activity.

## METHODS

### Population sample

This study is based on *SEPAGES-feasibility* cohort (*Suivi de l'Exposition à la Pollution Atmosphérique durant la Grossesse et Effets sur la Santé*; Assessment of air pollution exposure during pregnancy and effect on health). SEPAGES is a couple-child cohort on pre- and postnatal environmental determinants of fetus and infant development and health. In the feasibility study, women with singleton pregnancy living in Grenoble were recruited in obstetrical practices before 17 gestational weeks (calculated from the date of the last menstrual period) between July 2012 and July 2013. Grenoble is a flat urban area of about 670,000 inhabitants surrounded by the Alps, with a marine West Coast climate, a warm summer and no dry season. The inclusion criteria were that women had to be 18 years old or more, speak and write French, plan to give birth in one of the four maternity wards of the Grenoble urban area, and to be enrolled in the French social security system. The study was approved by the relevant ethical committees (CPP, Comité de Protection des Personnes Sud-Est; CNIL, Commission Nationale de l'Informatique et des Libertés; CCTIRS, Comité Consultatif sur le Traitement de l'Information en matière de Recherche dans le domaine de la Santé; ANSM, Agence Nationale de sécurité du Médicament et des produits de santé). All participating women and their partners gave informed written consent for their own participation.

### Study design

At each trimester of pregnancy, measurements of space-time activity and air pollution were performed for 7 consecutive days. Women were asked to carry a GPS device and filled in a detailed activity diary (n=40); a subsample of women were asked to carry a NO<sub>2</sub> passive sampler (n=10) and have a personal PM<sub>2.5</sub> monitor installed in their home (n=9).

## Space-time activity assessment

During one week at each trimester, pregnant women filled in a detailed activity diary to record their locations (home indoor/outdoor; work indoor/outdoor; other indoor/outdoor) and transport mode (Supplementary Figure A.1). We manually geocoded the home and work addresses using the free on-line French cadastral maps (<http://www.cadastre.gouv.fr/>) (Jacquemin et al., 2013).

During the same three weeks, women carried a GPS device (*GlobalSat* model DG-100 for 94% of the measurement weeks, or smartphone Samsung Galaxy ACE2 with *airplane* mode turned on, which recorded their position every 30 s and 1 s, respectively). Women were asked to carry the GPS device constantly with them when they were not home.

GPS data were cleaned in three main steps: (1) cleaning based on speed: if the speed estimated between two consecutive GPS records was larger than 170 km/h (maximum speed of regional trains), the second point was considered an outlier and deleted; (2) imputation of missing data: to handle the issue of GPS not working for a duration of up to 4 h, we replaced missing data using the last non-missing coordinate, provided that the next non-missing coordinate was located within 100 m from the first next recorded location; (3) cleaning of locations close to the home address (“Home buffer”): during daytime, all points located within a 100-meter buffer from home were replaced by the home address; this distance was increased to 200 m at night. This was meant to account for the GPS signal “bouncing”, which happens when the GPS device is inside a building. Moreover, when the first point of the day was inside the home buffer, we considered that the woman had spent her night at home (from midnight); similarly, if the last GPS point of the day was inside the buffer, we considered that the woman stayed home until midnight. When we did not have information for the entire night, we assumed that the woman was home from 10 p.m to 6 a.m.

## Pollutants concentrations

We considered two pollutants: PM<sub>2.5</sub> and NO<sub>2</sub>. Hourly PM<sub>2.5</sub> and NO<sub>2</sub> measurements of the monitoring station closest to the volunteer's home address were used as a first approach. There were three ambient monitoring stations measuring NO<sub>2</sub> and one background station measuring PM<sub>2.5</sub> in the Grenoble urban area.

PM<sub>2.5</sub> and NO<sub>2</sub> yearly concentrations were also obtained with a finer spatial resolution by combining two dispersion models developed for the year 2012, one covering the Grenoble urban area with a fine spatial resolution (10×10 meter grid, SIRANE model), and one covering the rural areas of Rhône-Alpes region (Figure 1), with a kilometric resolution (PREVALP model) (Soulhac et al., 2012, 2011). To obtain hourly concentrations at each location, we applied a previously defined approach relying on the hourly measurements from a background monitoring station (Lepeule et al., 2010; Pedersen et al., 2013; Slama et al., 2007a): we multiplied the yearly levels at each location by an hourly ratio  $C_{\text{hourly}}/C_{\text{yearly}}$ , where  $C_{\text{hourly}}$  and  $C_{\text{yearly}}$  corresponded to hourly concentrations and annual mean concentration respectively, both observed during the year 2012 in “Grenoble les Frênes” background station.

The same weeks the women carried the GPS device, a subsample of 10 non-smoking pregnant women carried (hanging on their bag or clothes) a NO<sub>2</sub> passive air sampler (Passam tube, Passam AG, Männedorf, Switzerland). The air sampler collected NO<sub>2</sub> by molecular diffusion along an inert tube to an absorbent (triethanolamine); the concentration of NO<sub>2</sub> was later determined by spectrophotometrical method (Hafkenscheid et al., 2009).

For 9 non-smoking pregnant women of the same subsample, we measured indoor PM<sub>2.5</sub> at home during the same weeks of the second and third trimesters of pregnancy when the GPS device was carried, using environment monitors (*p*DR1500, Thermo Fisher Scientific, Massachusetts, USA), estimating mass concentration by nephelometry. The device installed in the main room about one meter above the floor recorded indoor concentration every 10 min over the measurement week.

### Exposure models

From the above mentioned measurements, we developed 8 models to characterize exposure to PM<sub>2.5</sub> and NO<sub>2</sub> (Table 1).

- Station-based static outdoor model (M1): exposure corresponded to the trimester-specific average of the hourly measurements of atmospheric pollutants by the background air monitoring station closest to the volunteer's home address (using QGIS 2.2.0-Valmiera). Model M1 was a purely temporal model for PM<sub>2.5</sub> since it relied on a unique station.
- Dispersion-based static outdoor model (M2): exposure corresponded to the estimate from the dispersion model at the home address. Compared to M1, M2 had a much finer spatial resolution.
- Space-time activity outdoor models (M3 and M4): we averaged outdoor air pollution levels estimated from the dispersion model at each location where the woman spent time. Space-time activity was either based on raw (M3) or cleaned (M4) GPS data. M3 and M4 were used to evaluate the impact of integrating space-time activity compared to M2.
- GPS and diary space-time activity model (M5): since the procedure used to clean GPS data in model M4 still left missing data, we further used the data from the diary filled in by the pregnant women during the week of measurements to locate women at home or at work when GPS data were missing.
- Static indoor model (M6, PM<sub>2.5</sub> only): exposure corresponded to the average of indoor PM<sub>2.5</sub> levels estimated by the home active PM<sub>2.5</sub> sampler.
- Dynamic model taking into account outdoor and indoor concentrations of air pollutants (M7, PM<sub>2.5</sub> only): concentration corresponded to a time-weighted average of indoor levels (when the woman was home; M6) and seasonalized outdoor levels from dispersion models (when the woman was outside home); space-time activity was assessed using clean GPS data and data from the diary filled in by the pregnant women (M5). M7, which incorporates indoor levels and fine-scale outdoor levels, corresponded to what we expected to be the best approach model.

- Personal passive air sampler (M8, NO<sub>2</sub> only): exposure corresponded to the mean concentration of NO<sub>2</sub> estimated by the passive air sampler carried by the woman during 7 consecutive days.

For models M2 to M8, after having estimated pregnant women's exposures at each week of measurement, we converted all exposures to trimester estimates using data from the Grenoble background monitoring station "Grenoble les Frênes" to calculate a temporal ratio  $C_{\text{trimester}}/C_{\text{weekly}}$ , where  $C_{\text{trimester}}$  corresponded to the mean concentration of atmospheric pollutants during the trimester of pregnancy and  $C_{\text{weekly}}$  corresponded to the mean concentration during the week of measurement; consequently, the models' estimates were meant to represent each trimester of pregnancy (92 days for trimesters 1 and 2) which are of relevance for further studies of birth outcomes in relation to atmospheric pollution.

### Statistical analysis

We considered 4 time windows of exposure: the entire pregnancy and each trimester of the pregnancy; for indoor PM<sub>2.5</sub> levels (M6 and M7), no data for trimester 1 were available. Mean, standard deviation and 25<sup>th</sup>, 50<sup>th</sup>, 75<sup>th</sup> percentiles of each model's estimates were reported. Scatter plots were used for visual comparison of the models' estimates. We compared the estimates from the various exposure models using Spearman's rank correlation coefficients ( $r$ ) and paired t-tests. We also assessed the concordance between exposure estimates categorized in tertiles through Kappa coefficient ( $K$ ). All descriptive statistics, Spearman's rank correlation coefficients and concordances between exposure estimates during weeks of measurements without temporal adjustment for trimester are presented in the supplementary data. Analyses were performed with STATA 12 (StataCorp. 2011. *Stata Statistical Software: Release 12*. College Station, TX).

## RESULTS

### Study population

Among the 40 women recruited in SEPAGES-feasibility cohort, 31 women had GPS tracking data for all trimesters (78%), 5 for two trimesters (13%) and 4 for one trimester only (10%). All trimesters were not completed for all women because of the woman being included too late for trimester 1 measurements ( $n=4$ ), giving up or being lost to follow-up ( $n=4$ ), or being hospitalized ( $n=1$ ). Two women (5%) changed home during pregnancy, one of which moved out of the Grenoble urban area, impeding further assessment of exposure. The characteristics of the study population are described in Table 2. Volunteers were all in a relationship, their median age was 30 years (25<sup>th</sup>, 75<sup>th</sup> percentiles: 27, 32); most of them (60%) were nulliparous, employed (88%) and with a high socio-professional status (70%). The volunteers' home was on average 2.1 km (standard deviation, SD: 1.6 km) and 3.5 km (SD: 2.2 km) away from the nearest background station measuring NO<sub>2</sub> and PM<sub>2.5</sub>, respectively; they were on average 514 m (SD: 460 m) distant from the nearest major road (including expressway, primary/secondary highway and arterial road).



### Impact of improving the spatial resolution of models on exposure estimates

Mean pregnancy exposure levels, as estimated from the static outdoor model relying only on the nearest background air monitoring station (M1), were 17.8  $\mu\text{g}/\text{m}^3$  for  $\text{PM}_{2.5}$  (SD: 2.5  $\mu\text{g}/\text{m}^3$ ; Table 3) and 24.1  $\mu\text{g}/\text{m}^3$  for  $\text{NO}_2$  (SD: 5.8  $\mu\text{g}/\text{m}^3$ ; Table 4). The outdoor static model relying on the dispersion modeling (M2) yielded higher average levels (18.5  $\mu\text{g}/\text{m}^3$ , SD: 2.6  $\mu\text{g}/\text{m}^3$  for  $\text{PM}_{2.5}$ ; 29.0  $\mu\text{g}/\text{m}^3$ , SD: 4.5  $\mu\text{g}/\text{m}^3$  for  $\text{NO}_2$ ;  $p < 0.001$ ), compared to M1. Improving the spatial resolution of the outdoor model had a minor impact for  $\text{PM}_{2.5}$  and a moderate impact for  $\text{NO}_2$ : the correlations between the entire pregnancy estimates from models M1 and M2 were 0.93 for  $\text{PM}_{2.5}$  ( $p < 0.001$ ; Table 5) and 0.67 for  $\text{NO}_2$  ( $p < 0.001$ ; Table 6).

### Impact of incorporating space-time activity on exposure estimates

Mean pregnancy exposures incorporating space-time activity assessed using raw GPS data (M3) were 18.0  $\mu\text{g}/\text{m}^3$  (SD: 3.4  $\mu\text{g}/\text{m}^3$ ) for  $\text{PM}_{2.5}$  and 29.6  $\mu\text{g}/\text{m}^3$  (SD: 6.3  $\mu\text{g}/\text{m}^3$ ) for  $\text{NO}_2$ . On average, 70% (SD: 24%) of raw GPS data were missing (Supplementary Table A.5). After deleting the GPS data considered as outliers (1,562 data out of the 680,040 raw GPS points, 0.23%), and imputing missing values with our cleaning algorithm, the proportion of missing points decreased to 31% (SD: 11%; model M4). The outdoor exposure model incorporating space-time activity with the cleaned GPS data (M4) had estimated pregnancy levels of 18.6  $\mu\text{g}/\text{m}^3$  (SD: 2.8  $\mu\text{g}/\text{m}^3$ ) for  $\text{PM}_{2.5}$  (Table 3) and 27.7  $\mu\text{g}/\text{m}^3$  (SD: 4.8  $\mu\text{g}/\text{m}^3$ ) for  $\text{NO}_2$  (Table 4). The correlation coefficients between M4 and M3 estimates were 0.77 ( $p < 0.001$ ) for  $\text{PM}_{2.5}$  and 0.90 ( $p < 0.001$ ) for  $\text{NO}_2$ .

The GPS data cleaning process had a rather strong impact on the exposure estimates: the correlations between models M2 and M4 (using clean GPS data) were 0.93 for  $\text{PM}_{2.5}$  and 0.94 for  $\text{NO}_2$  ( $p < 0.001$ ; Figure 2), while the correlations between M2 and M3 (using raw GPS data) were lower (0.77 for  $\text{PM}_{2.5}$  and 0.83 for  $\text{NO}_2$ ;  $p < 0.001$ ).

The median time spent at home averaged over the entire pregnancy and estimated from the activity diary was 16.3 h per day (25<sup>th</sup>, 75<sup>th</sup> percentiles: 14.8 h, 18.2 h). The estimate based on the clean GPS data was lower (median, 13.4 h; 25<sup>th</sup>, 75<sup>th</sup> percentiles: 11.7 h, 14.7 h), possibly as a consequence of GPS data being more frequently missing when subjects were home. Time spent at home estimated using information from diary filled in by the volunteers increased from 15.0 and 15.2 h per day in trimesters 1 and 2 to 18.1 h in trimester 3, when maternity leave usually starts in France (Supplementary Table A.5).

Combining the information from diaries filled in by the volunteers to clean GPS data (M5) further decreased the proportion of missing data on space-time activity to 7% of the measurement weeks (SD: 6%); the median time spent at home, as estimated from clean GPS data combined to diaries, was 18.5 h (25<sup>th</sup>, 75<sup>th</sup> percentiles: 16.9 h, 19.7 h; M5; Supplementary Table A.5). The mean pregnancy levels estimated by this model were 18.5  $\mu\text{g}/\text{m}^3$  (SD: 2.6  $\mu\text{g}/\text{m}^3$ ) for  $\text{PM}_{2.5}$  and 28.9  $\mu\text{g}/\text{m}^3$  (SD: 4.6  $\mu\text{g}/\text{m}^3$ ) for  $\text{NO}_2$ . This model had a high correlation with the static dispersion model at the home address (M2) (0.97 for  $\text{PM}_{2.5}$  and 0.98 for  $\text{NO}_2$ ;  $p < 0.001$ ; Figure 3), showing little impact of the incorporation of space-time activity on exposure estimates.



For both pollutants, results by trimester of pregnancy were similar to those for the entire pregnancy (Table 3 Table 4 Table 5 Table 6).

Compared to models temporally-corrected (converted to trimester estimates; Table 3 for PM<sub>2.5</sub>; Table 4 for NO<sub>2</sub>), models M1 to M5 (outdoor models) without temporal adjustment had higher variability, while models M6 to M8 (including indoor or personal measurements) had a smaller variability (Supplementary Table A.1 for PM<sub>2.5</sub> and Table A.2 for NO<sub>2</sub>). Correlations between week-specific models (Supplementary Table A.3 for PM<sub>2.5</sub> and Table A.4 for NO<sub>2</sub>) were higher than the correlations between trimester-specific models (Table 5 for PM<sub>2.5</sub>; Table 6 for NO<sub>2</sub>), as a consequence of temporal variations having a greater influence on week-specific compared to trimester specific models.

### Impact of incorporating indoor PM<sub>2.5</sub> levels on exposure estimates

The median duration of time spent at home for the 9 non-smoking women in which indoor PM<sub>2.5</sub> levels were assessed during the second and third trimesters was 19.2 h per day (25<sup>th</sup>, 75<sup>th</sup> percentiles: 17.5 h, 19.8 h), as estimated from the clean GPS data and the activity diary. Supplementary Figure A.3 displays the PM<sub>2.5</sub> home levels during one week for one subject. The weekly home average indoor PM<sub>2.5</sub> level (model M6) was 16.8 µg/m<sup>3</sup> (SD: 4.8 µg/m<sup>3</sup>; Table 3). The correlation between the average of the second and third trimesters estimates from the outdoor static dispersion model at the home address (M2) and home indoor levels averaged during these two trimesters (M6) was 0.50 (p=0.17; Table 5).

PM<sub>2.5</sub> mean pregnancy level estimated using clean GPS data and incorporating indoor levels when the woman was home and outdoor estimates when she was outside (M7), which we considered our “best approach model” for PM<sub>2.5</sub>, was 18.8 µg/m<sup>3</sup> (SD: 3.5 µg/m<sup>3</sup>). Correlations between M7 and estimates based on the average of the entire pregnancy from both models using clean GPS data were 0.25 for M4 (p=0.52) and 0.47 for M5 (p=0.21), (Figure 4), while the correlations between M7 and the static outdoor models were 0.40 for M1 (p=0.29) and 0.35 for M2 (p=0.36), showing that incorporating indoor levels strongly modified the estimated exposure.

### Personal versus modeled NO<sub>2</sub> levels

The mean NO<sub>2</sub> concentration estimated by the personal passive air samplers carried by 10 non-smoking women was 23.9 µg/m<sup>3</sup> (SD: 4.9 µg/m<sup>3</sup>; M8). In this subsample, 7 women out of 10 used gas-stove for cooking at home during the period of measurements; in this group NO<sub>2</sub> levels tended to be higher (28.6 µg/m<sup>3</sup>, SD: 3.0 µg/m<sup>3</sup>; n=7) than in the group not using gas for cooking (22.3 µg/m<sup>3</sup>, SD: 2.6 µg/m<sup>3</sup>; n=3; p=0.02). Personal NO<sub>2</sub> measurements (M8) were not correlated with models based on outdoor NO<sub>2</sub> levels without space-time activity (r=0.03 for M1, p=0.93; and r=-0.16 for M2, p=0.65) and, if anything, tended to be negatively correlated with models incorporating space-time activity with clean GPS data (r=-0.42 for M4, p=0.23; r=-0.39 for M5, p=0.26; Figure 5).

## DISCUSSION

To our knowledge this study is one of the first to compare air pollution exposure models combining modeled outdoor air pollution levels, GPS-based space-time activity data and

indoor and personal air pollution measurements among pregnant women. Improving the spatial resolution of the outdoor environmental model (between M1 and M2) had a minor impact for PM<sub>2.5</sub> and a moderate impact for NO<sub>2</sub>. The proportion of missing data was high in raw GPS data; we proposed a simple algorithm allowing to clean these data. Integrating the space-time activity (after cleaning) to the outdoor exposure model modified to a very limited extent PM<sub>2.5</sub> and NO<sub>2</sub> exposure levels estimated at the home addresses, as shown by the very high correlations between estimates from M2 and M5 models. Models using outdoor levels of air pollutants (M1 to M5; without considering M3) were weakly to moderately correlated ( $r=0.25$  to  $0.47$ ;  $n=9$ ) with models incorporating PM<sub>2.5</sub> indoor measurements (M7) and not correlated ( $r=-0.42$  to  $0.03$ ;  $n=10$ ) with NO<sub>2</sub> measurements from personal passive air samplers (M8).

### **Impact of improving the spatial resolution of models on exposure estimates**

The correlation between PM<sub>2.5</sub> exposure estimates from both static models (model M1, relying only on values estimated with the nearest background air monitoring station, and M2 using the dispersion model estimate at the home address) was high. This correlation tended to be lower for NO<sub>2</sub> estimates, which may be explained by the stronger spatial variability of NO<sub>2</sub> compared to PM<sub>2.5</sub> concentrations as estimated by the dispersion model in the urban area (interquartile range on annual concentration on the dispersion model during the year 2012:  $0.6 \mu\text{g}/\text{m}^3$  for PM<sub>2.5</sub> and  $3.1 \mu\text{g}/\text{m}^3$  for NO<sub>2</sub>). These results are in line with a study in two other French metropolitan areas which reported correlations between home's nearest air quality monitoring station and dispersion model's estimates of 0.63 to 0.71 for NO<sub>2</sub>, depending of the buffer size around monitoring stations (1 to 5 km); and of 0.81 to 0.85 for PM<sub>10</sub> (no estimate was provided for PM<sub>2.5</sub>) (Sellier et al., 2014). Other studies reported a limited spatial variability for PM<sub>2.5</sub> across urban areas (Eeftens et al., 2012; Martuzevicius et al., 2004), while a higher spatial variability was found for NO<sub>2</sub> (Cyrus et al., 2012). In this context of very low spatial contrasts for PM<sub>2.5</sub>, it is not surprising that time (of the measurement period) rather than location drives the estimated levels. Coherently, correlations between week-specific models were higher than correlations between trimester-specific models. An explanation is that the contribution of temporal variations to the overall variability in exposure is smaller when longer time periods are considered.

We seasonalized estimates using the hourly concentration of pollutants from the representative background monitoring station, assuming that the variation of air pollutants over time was spatially homogeneous (Lepeule et al., 2010; Slama et al., 2007a).

### **Impact of incorporating space-time activity on exposure estimates**

Our model using outdoor air pollution at the home address (M2) was highly correlated with the two models incorporating clean GPS data (M4 and M5). This can be explained by the relatively high proportion of time spent at home by the pregnant women (77% as estimated by combining GPS and diary data, M5), which limits any impact of outdoor exposures at other locations than home. These results are in agreement with one Canadian study on pregnant women which used GPS-based space-time activity, LUR models and ambient monitoring data; the correlations between the model using the full GPS route data and the

model using only home locations were high for NO, NO<sub>2</sub>, PM<sub>2.5</sub> ( $r=0.83-0.92$  according to pollutant;  $n=35$ ) (Nethery et al., 2008b).

In our study, for some women the GPS device stopped to record the position for a moment during the day, typically when women were indoors, which is a well-known limitation of GPS devices (Maddison and Ni Mhurchu, 2009) not embedded in smartphones. The overall average of missing values in the raw GPS data was high (70%), as a result of the high proportion of time spent indoors by the pregnant women. Geolocalization errors are generally larger in indoors environments than outdoors (Beekhuizen et al., 2013; Elgethun et al., 2003; Schutz and Chambaz, 1997; Wu et al., 2010). We implemented a simple algorithm to impute missing GPS points, which decreased the average of missing values to 31% of the measurement weeks. Previous studies used various cleaning algorithms (Breen et al., 2014; Dias and Tchepel, 2014; Gerharz et al., 2013; Maddison et al., 2010; Nethery et al., 2008b; Wiehe et al., 2008). One study replaced missing data using the last value carried forward provided the next value was within 100 m of the last value (Maddison et al., 2010). Another study assigned all GPS points within 350 m of residence as home (Nethery et al., 2008b). In our study we used both of the aforementioned approaches for missing data imputation, with the difference that the accuracy of our devices allowed us to decrease the buffer around the home to 100 m for the day and 200 m for the night. Two studies built an algorithm that considered a measurement as valid depending on the number of satellites from which the GPS received a signal and on the dilution of precision value (Breen et al., 2014; Dias and Tchepel, 2014); in our study we did not have access to this information. Developing a cleaning algorithm might seem cumbersome but it allows automatization of the cleaning process; even if the use of GPS tracking data showed a limited impact on the exposure model using only home addresses, it allows us to develop a more dynamic and realistic model for the estimation of exposure to atmospheric pollutants. The model using the clean GPS data (M4) better correlated with the model not accounting for space-time activity (M1 and M2) than the one using the raw GPS data (M3). This illustrates that the GPS data cleaning process, which leads to a strong increase in the estimated proportion of time spent home, is an important step in the estimation of exposure to atmospheric pollutants. In our setting, examination of the correlations between the various models suggests that the use of raw GPS data induced more exposure misclassification in the outdoor estimates than the estimates totally ignoring space-time activity.

Exposure to traffic-related air pollution during commuting also contributes to personal exposures (Gulliver and Briggs, 2005). This exposure is related to the transportation mode; car users tend to experience the highest exposure compared to walkers, bus or bike users (de Nazelle et al., 2012; Zurbier et al., 2010). Since GPS devices were not able to differentiate travels by car, bus or other means of transportation, and since we could not assess personal exposures while commuting, we assumed that the concentration of atmospheric pollutant during commuting corresponded to the outdoor level, which has probably led to an underestimation of the impact of exposures during commuting in our study.

The activity diary filled in by the volunteers allowed to further limit missing data on space-time activity when the GPS device failed to geolocalize subjects. One limitation of paper diaries is their inability to easily provide geolocalization during commuting, but we believe

that they are a very relevant complement to the GPS data. Using WiFi-enabled smartphones represents another option with an expected lower rate of missing values indoors compared to the GPS devices we used. However, the use of smartphones not in the *airplane* mode may raise data privacy issues (as the smartphone information may be collected) and possibly ethical issues, as there is some concern regarding the possible health effects of electromagnetic fields, particularly during pregnancy.

### Impact of incorporating indoor PM<sub>2.5</sub> levels on exposure estimates

In our study, indoor home PM<sub>2.5</sub> concentrations tended to be lower than outdoor concentrations. Brunekreef *et al.* reported that in Helsinki and Amsterdam, the median PM<sub>2.5</sub> concentrations were lower indoor than outdoor (Brunekreef *et al.*, 2005). One Canadian study using the *pDR1500* device in the measurement of personal PM<sub>2.5</sub> exposure reported that the lowest concentrations were measured when participants were indoor at home (Van Ryswyk *et al.*, 2014). One study in Barcelona, Spain conducted on 54 pregnant women reported a higher PM<sub>2.5</sub> level indoors than outdoors (Schembari *et al.*, 2013); this result differs from our study and studies aforementioned, this might be explained by the different climate and probably ventilation rate compared with Northern cities.

In our study, the correlation between outdoor PM<sub>2.5</sub> estimates at the home address (M2) and indoor home levels (M6) was low (in the 0.03-0.50 range). Similarly, the correlation between the outdoor model incorporating space-time activity (M5) and the model further integrating indoor measurements (M7) was low (in the -0.12-0.47 range). Both correlations tended to be higher during the second trimester than the third; the longer time spent at home during the third trimester may explain the weaker correlation between outdoor estimates and estimates incorporating indoor levels. Given the limited sample size (n=9), these results should be considered with caution. The study relying on 2-day indoors and outdoors PM<sub>2.5</sub> measurements in 54 pregnant women living in Barcelona reported a strong correlation between indoor and outdoor levels (Spearman's rank correlation, 0.63) (Schembari *et al.*, 2013), which might be explained by the different climates, and by the fact that indoor and outdoor measurements were performed with the same gravimetric devices. These short-term correlations (in which temporal variations have a strong impact) cannot be compared to our longer-term estimates, which were the focus of our study because of the possible effects of chronic exposure to air pollution during pregnancy.

The outdoor and indoor PM<sub>2.5</sub> estimates relied on different approaches, which may have impacted between-model differences and their correlations. Outdoor concentrations were obtained using gravimetric FDMS-TEOM monitors (Filter Dynamics Measurements System-Tapered Element Oscillating Microbalance) which do not take the aqueous component of PM into account (particle-associated water); indoor concentrations were estimated using a nephelometric measurement which depends on humidity level (due to water absorbed in the particles), and on the distribution of size, shape, and refractive index of the particles, which varies according to sources (Cropper *et al.*, 2013; Soneja *et al.*, 2014; Wallace *et al.*, 2003). Moreover, nephelometric devices not using filters allowing explicit weighing of PM<sub>2.5</sub>, as is the case of the device we used, make some assumptions on the size and mass distribution of local PM<sub>2.5</sub> which theoretically require calibration in each new

micro-environment and may induce spurious differences with measurements from monitoring stations. Besides differences in measurement techniques, there are real reasons why outdoor PM<sub>2.5</sub> levels and estimates incorporating indoor levels can differ; indoor PM<sub>2.5</sub> levels are generally influenced by sources and activities such as cooking, candle burning, smoking and by the type and frequency of ventilation (McCormack et al., 2008; Meng et al., 2009), in addition to outdoor levels. We included non-smoking women possibly exposed to environmental tobacco smoke, which constitutes a source of indoor pollution of fine particles. Since outdoors and indoors PM<sub>2.5</sub> may differ in physical and chemical nature (Habre et al., 2014; Kelly and Fussell, 2012) and hence possibly in terms of health effects, assessing exposure of PM<sub>2.5</sub> through active air samplers, to collect and later chemically analyze PM<sub>2.5</sub>, may be a good option when considering effects on a specific health parameter. Alternatively, if one is not interested in indoor sources of PM, or considers that they may have different health impact than PM from outdoor sources, then personal monitoring may not be the right option, unless the personal monitor is used to derive estimates of personal indoor and outdoor exposures separately (and additional information on outdoor levels when the woman is home are available).

Our results, with former studies (Baxter et al., 2007; Ozkaynak et al., 2013), suggest that reliance on outdoor levels only in environmental epidemiology implies a high degree of exposure misclassification if PM<sub>2.5</sub> as a whole (whatever their source) is the focus of the study. This may particularly hold for pregnant women, who may have different activity patterns and spend more time at home compared to the general population (Nethery et al., 2008a, 2008c).

### Personal versus modeled NO<sub>2</sub> levels

For NO<sub>2</sub>, personal exposure assessed from a personal passive air sampler (M8) was poorly, if at all, correlated with our model based on outdoor modeled values and incorporating space-time activity but not considering indoor levels (M4 and M5), suggesting that personal exposure cannot be estimated by outdoor levels in this setting. Again, this result was based on a small population (n=10). The mean NO<sub>2</sub> concentration estimated by the personal passive air samplers was lower than outdoor exposure estimates using space-time activity by about 10%. This is consistent with a Canadian study on 62 pregnant women in which personal NO<sub>2</sub> exposure decreased with increasing time spent at home and had a low correlation with the value predicted at the home address (r=0.18 using LUR model; r=0.05 using outdoor monitoring stations) (Nethery et al., 2008b). Two other studies among pregnant women conducted in Spanish cities assessed personal exposure to NO<sub>2</sub> and outdoor levels of NO<sub>2</sub> using permanent monitoring stations; correlations were 0.58 for 1-week sampling in Barcelona (Schembari et al., 2013) and 0.39 for a 48 h sampling in Sabadell (Valero et al., 2009).

In our study the use of a gas-stove was associated with a higher NO<sub>2</sub> personal level (based on a small population). This is in agreement with previous studies reporting that gas cooking influences personal NO<sub>2</sub> exposure (Kousa et al., 2001; Valero et al., 2009).

## Conclusion

Our results confirm that it is possible to use GPS tracking data to provide an individual estimate of exposure to atmospheric pollutants, provided that GPS data are cleaned. In this urban area, incorporation of space-time activity only very slightly modified the estimated outdoor exposure to PM<sub>2.5</sub> and NO<sub>2</sub>. In a subgroup of subjects, exposure estimates incorporating indoor levels were poorly correlated with the estimated exposure considering only outdoor air pollutants, so that future studies interested in effects of chronic (as opposed to short-term) exposure to PM<sub>2.5</sub> and NO<sub>2</sub> from all sources altogether should consider incorporating estimates of personal exposure or indoor levels.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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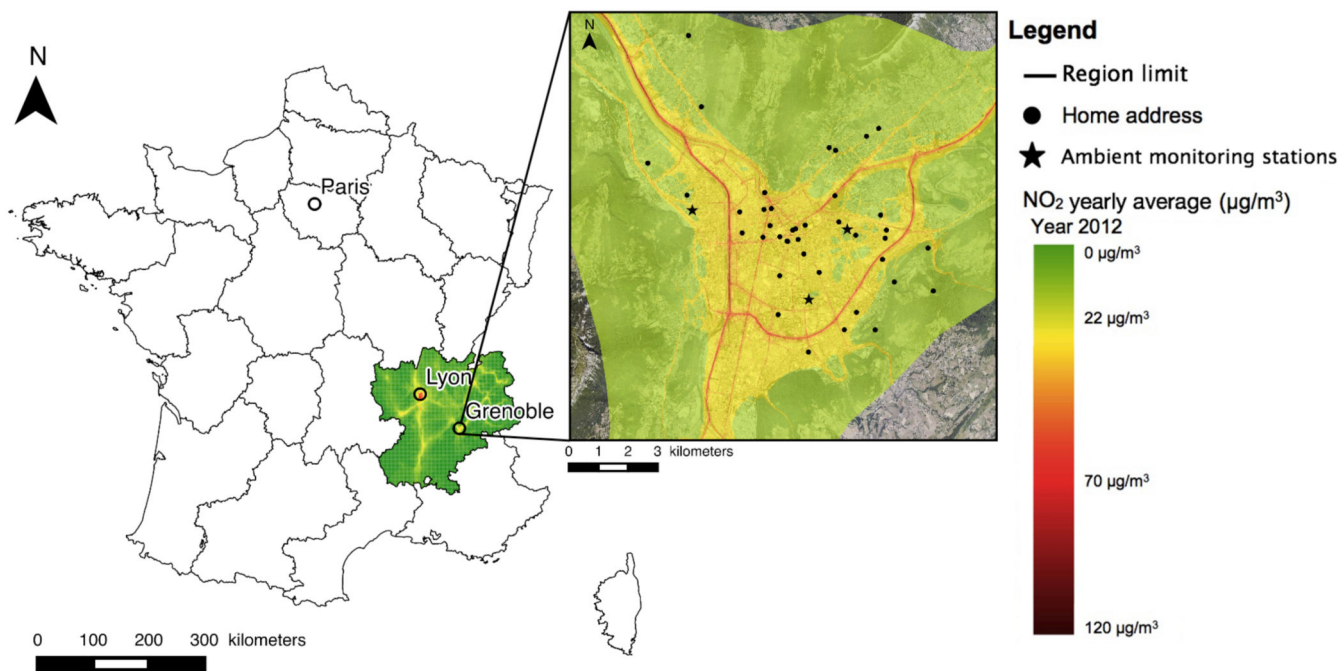


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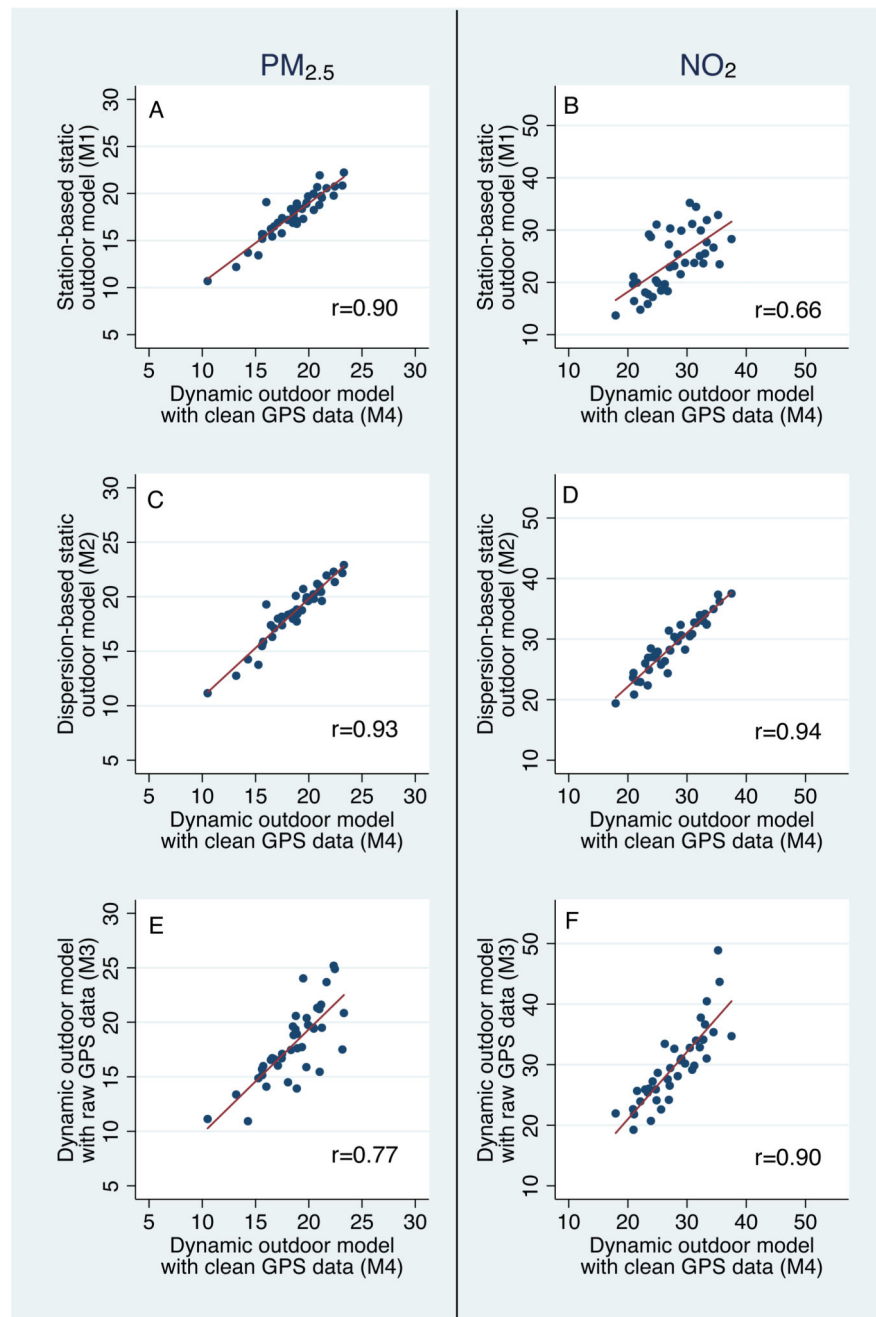
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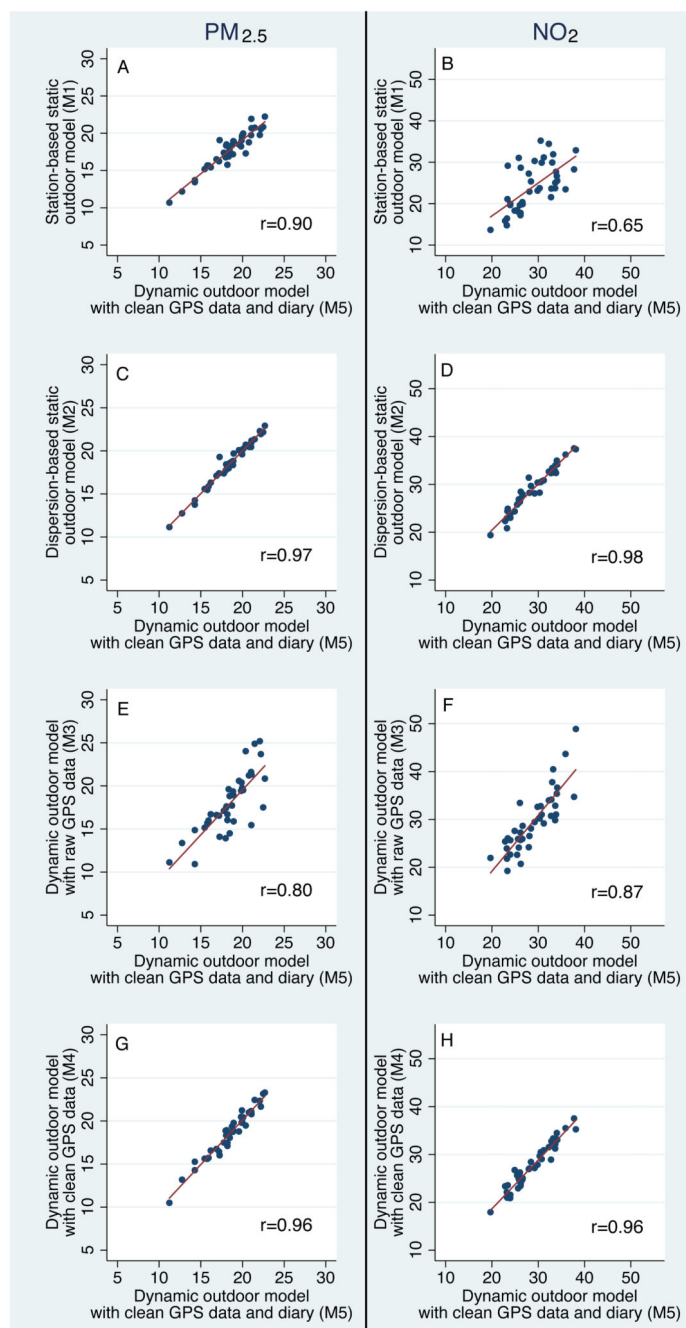


**Figure 1.** NO<sub>2</sub> mean annual estimated from dispersion models in Rhône-Alpes region (left panel, PREVALP dispersion model, 1 km grid) and the Grenoble urban area (right panel, SIRANE dispersion model, 10 m grid), together with the volunteers' home addresses. Home address locations were randomly moved by a few hundred meters to protect subjects' privacy.

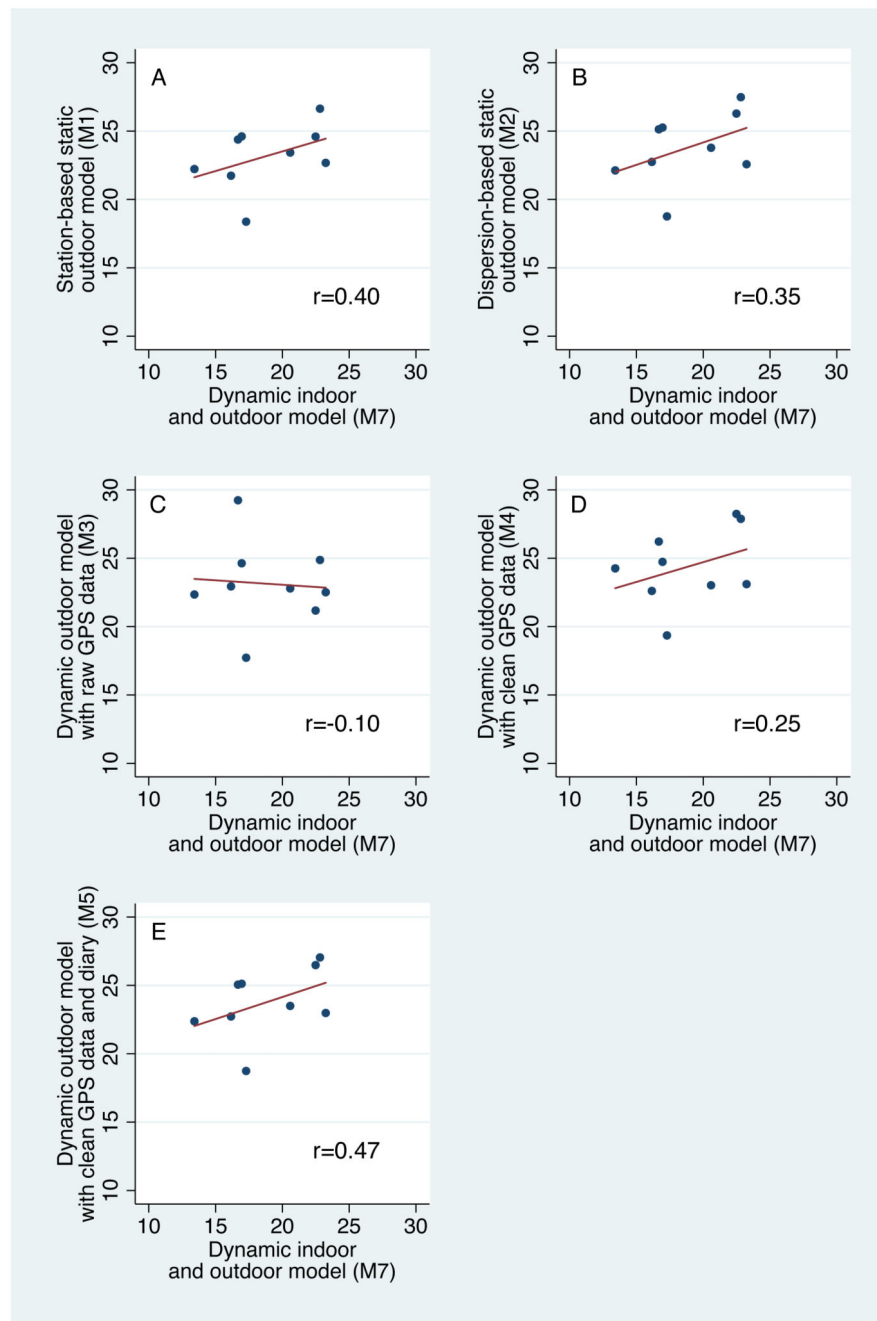


**Figure 2.** Scatter plots of model M4 (Dynamic outdoor model with clean GPS data) versus: A and B: model M1 (Station-based static outdoor model); C and D: model M2 (Dispersion-based static outdoor model); E and F: model M3 (Dynamic outdoor model with raw GPS data) exposure estimates. Each point corresponds to the pregnancy average exposure ( $\mu\text{g}/\text{m}^3$ ) (N=40).



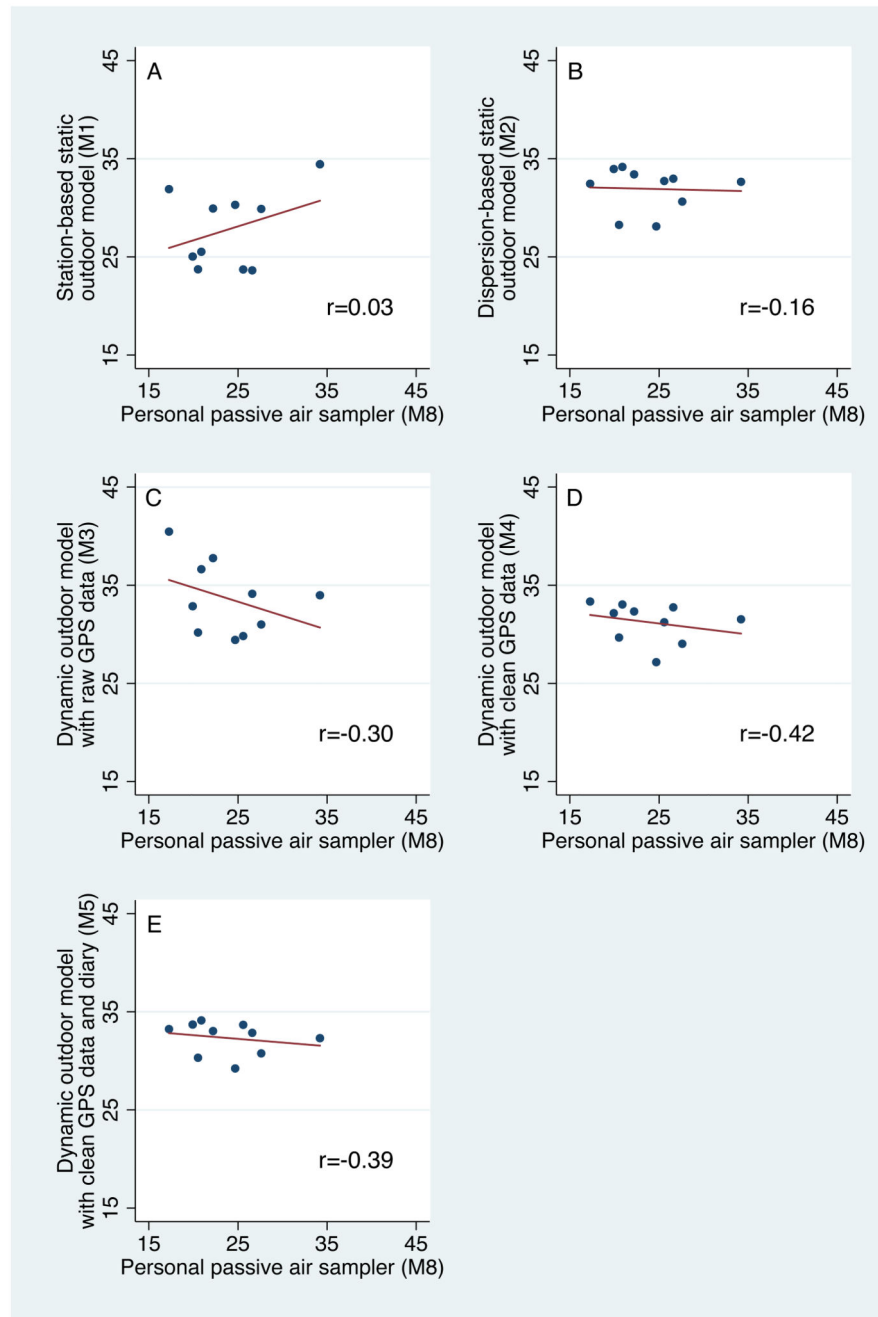


**Figure 3.** Scatter plot of model M5 (Dynamic outdoor model with clean GPS data and diary) versus: A and B: model M1 (Station-based static outdoor model); C and D: model M2 (Dispersion-based static outdoor model); E and F: model M3 (Dynamic outdoor model with raw GPS data); G and H: model M4 (Dynamic outdoor model with clean GPS data). Each point corresponds to the pregnancy average exposure ( $\mu\text{g}/\text{m}^3$ ) ( $N=40$ ).



**Figure 4.**

PM<sub>2.5</sub> exposure estimates – Scatter plots of model M7 (Dynamic indoor and outdoor model) versus: A: model M1 (Station-based static outdoor model); B: model M2 (Dispersion-based static outdoor model); C: model M3 (Dynamic outdoor model with raw GPS data); D: model M4 (Dynamic outdoor model with clean GPS data); E: model M5 (Dynamic outdoor model with clean GPS data and diary). Each point corresponds to the 2<sup>nd</sup> and 3<sup>rd</sup> trimester average exposure (µg/m<sup>3</sup>) (N=9).



**Figure 5.**  $\text{NO}_2$  exposure estimates – Scatter plots of model M8 (Personal passive air sampler) versus: A: model M1 (Station-based static outdoor model); B: model M2 (Dispersion-based static outdoor model); C: model M3 (Dynamic outdoor model with raw GPS data); D: model M4 (Dynamic outdoor model with clean GPS data); E: model M5 (Dynamic outdoor model with clean GPS data and diary). Each point corresponds to the pregnancy average exposure ( $\mu\text{g}/\text{m}^3$ ) (N=10).

**Table 1**  
Overview of the models used to estimate exposure to atmospheric pollutants in the SEPAGES-Feasibility cohort.

Model <sup>a</sup>	Outdoor pollution levels		Space-time activity			Indoor measurements	Personal dosimeter	Pollutants	N
	Background monitoring stations	Dispersion model	Not considered <sup>b</sup>	Raw GPS data	Clean GPS data				
M1. Station-based static outdoor model	X		X					PM <sub>2.5</sub> , NO <sub>2</sub>	40
M2. Dispersion-based static outdoor model		X	X					PM <sub>2.5</sub> , NO <sub>2</sub>	40
M3. Dynamic outdoor model with raw GPS data		X		X				PM <sub>2.5</sub> , NO <sub>2</sub>	40
M4. Dynamic outdoor model with clean GPS data		X			X			PM <sub>2.5</sub> , NO <sub>2</sub>	40
M5. Dynamic outdoor model with clean GPS data and diary		X				X		PM <sub>2.5</sub> , NO <sub>2</sub>	40
M6. Static indoor model			X			X		PM <sub>2.5</sub>	9
M7. Dynamic indoor and outdoor model		X				X	X	PM <sub>2.5</sub>	9
M8. Personal passive air sampler							X	NO <sub>2</sub>	10

<sup>a</sup>: All models were seasonalized using data from Grenoble background monitoring station so that the models estimates represent the trimester of pregnancy and not only the week of measurement.

<sup>b</sup>: Estimates are provided for the home address only, ignoring space-time activity. For M1, this corresponds to the nearest monitor's estimate.

**Table 2**

Characteristics of the population of 40 pregnant women.

	N	%
<b>Maternal age at conception</b>		
18-25 years	2	(5)
26-30 years	20	(50)
31-35 years	13	(33)
> 35 years	5	(12)
<b>Weeks of amenorrhea at inclusion</b>		
< 12 weeks	11	(28)
12 weeks	22	(55)
13 - 18 weeks	7	(18)
<b>Month of conception of the child</b>		
January-March	7	(18)
April-June	14	(35)
July-September	15	(38)
October-December	4	(10)
<b>Maternal parity before the index pregnancy</b>		
0	24	(60)
1 child	12	(30)
2 children	4	(10)
<b>Maternal age at the end of education (years)</b>		
18 - 20 years old	3	(8)
21 - 23 years old	17	(43)
23 - 25 years old	10	(25)
> 25 years old	4	(10)
Still studying	6	(15)
<b>Marital status</b>		
In relationship (cohabitation, married)	40	(100)
<b>Working status</b>		
Employed	35	(88)
Unemployed	2	(5)
Unknown	3	(8)
<b>Socio-professional status</b>		
High socio-professional status	28	(70)
Low socio-professional status	9	(23)
Unknown	3	(8)
<b>Area of residence</b>		
Grenoble city center	17	(43)
Suburban area	23	(58)
<b>Type of residence</b>		
House	7	(18)

	N	%
Apartment	28	(70)
Unknown	5	(13)
<b>Changed home during pregnancy</b>		
Yes	2	(5)
No	38	(95)
<b>Gas-stove at home</b>		
Yes	21	(53)
No	15	(38)
Unknown	4	(10)
<b>Maternal active smoking</b>		
Yes	6	(15)
No	31	(78)
Unknown	3	(8)
<b>Partner active smoking</b>		
Yes	8	(20)
No	25	(63)
Unknown	7	(18)
<b>Number of trimesters with GPS tracking data</b>		
1 trimester	4	(10)
2 trimesters	5	(13)
3 trimesters	31	(78)
<b>Indoor PM<sub>2.5</sub> measurements performed</b>	9	(23)
<b>Personal NO<sub>2</sub> measurements (PASSAM sampler) performed</b>	10	(25)



**Table 3**

Maternal PM<sub>2.5</sub> levels at each trimester and for the entire pregnancy estimated by the various exposure models considered ( $\mu\text{g}/\text{m}^3$ ).

Model and exposure window	N	mean	SD	(p25)	p50	p75)
<b>First trimester</b>						
M1. Station-based static outdoor model	36	18.5	5.1	(13.6	16.8	22.4)
M2. Dispersion-based static outdoor model	36	19.5	6.2	(14.1	17.0	23.9)
M3. Dynamic outdoor model with raw GPS data	36	18.8	7.1	(14.2	16.4	22.2)
M4. Dynamic outdoor model with clean GPS data	36	19.5	5.9	(14.5	17.5	22.3)
M5. Dynamic outdoor model with clean GPS data and diary	36	19.7	6.2	(14.3	17.1	23.9)
<b>Second trimester</b>						
M1. Station-based static outdoor model	38	17.7	6.4	(12.1	15.9	23.0)
M2. Dispersion-based static outdoor model	38	18.2	6.4	(12.4	16.2	23.7)
M3. Dynamic outdoor model with raw GPS data	38	17.7	7.4	(11.7	16.0	21.0)
M4. Dynamic outdoor model with clean GPS data	38	18.1	6.5	(12.4	16.3	24.1)
M5. Dynamic outdoor model with clean GPS data and diary	38	18.0	6.3	(12.5	15.3	23.7)
M6. Static indoor model	8	16.5	7.1	(10.1	16.2	20.0)
M7. Dynamic indoor and outdoor model	9	17.7	6.1	(13.8	14.5	20.1)
<b>Third trimester</b>						
M1. Station-based static outdoor model	33	17.8	6.8	(12.8	13.6	24.2)
M2. Dispersion-based model static outdoor model	33	18.8	6.9	(13.6	14.5	25.1)
M3. Dynamic outdoor model with raw GPS data	33	18.3	6.7	(14.1	15.9	22.5)
M4. Dynamic outdoor with clean GPS data	33	18.9	7.3	(13.5	15.1	25.7)
M5. Dynamic outdoor model with clean GPS data and diary	33	18.7	6.9	(13.6	14.6	25.4)
M6. Static indoor model	9	16.7	5.0	(14.7	19.2	19.6)
M7. Dynamic indoor and outdoor model	9	20.0	3.5	(18.2	20.7	22.0)
<b>Entire pregnancy <sup>a</sup></b>						
M1. Station-based static outdoor model	40	17.8	2.5	(16.4	18.3	19.6)
M2. Dispersion-based static outdoor model	40	18.5	2.6	(17.4	18.7	20.3)
M3. Dynamic outdoor model with raw GPS data	40	18.0	3.4	(15.8	17.6	20.1)
M4. Dynamic outdoor model with clean GPS data	40	18.6	2.8	(16.7	18.8	20.6)
M5. Dynamic outdoor model with clean GPS data and diary	40	18.5	2.6	(17.2	18.6	20.2)
M6. Static indoor model	9	16.8	4.8	(12.3	19.4	19.9)
M7. Dynamic indoor and outdoor model	9	18.8	3.5	(16.7	17.3	22.5)

<sup>a</sup>: Based on the average of the entire pregnancy for models M1 to M5, and on the average of 2<sup>nd</sup> and 3<sup>rd</sup> trimesters for models M6 and M7.

**Table 4**

Maternal NO<sub>2</sub> levels at each trimester and for the entire pregnancy estimated by the various exposure models considered ( $\mu\text{g}/\text{m}^3$ ).

Model and exposure window	N	mean	SD	(p25	p50	p75)
<b>First trimester</b>						
M1. Station-based static outdoor model	36	24.7	7.6	(19.9	24.1	27.5)
M2. Dispersion-based static outdoor model	36	29.4	5.8	(25.1	30.5	33.6)
M3. Dynamic outdoor model with raw GPS data	36	29.3	7.6	(25.9	30.1	33.8)
M4. Dynamic outdoor model with clean GPS data	36	27.8	5.6	(23.9	28.0	31.5)
M5. Dynamic outdoor model with clean GPS data and diary	36	29.4	5.4	(26.1	30.1	33.2)
M8. Personal passive air sampler	8	18.7	4.8	(15.7	18.0	20.9)
<b>Second trimester</b>						
M1. Station-based static outdoor model	38	25.6	11.3	(15.3	26.8	31.6)
M2. Dispersion-based static outdoor model	38	29.6	9.7	(19.5	30.9	38.0)
M3. Dynamic outdoor model with raw GPS data	38	30.2	12.3	(21.8	25.9	38.6)
M4. Dynamic outdoor model with clean GPS data	38	28.3	9.9	(19.0	27.4	37.4)
M5. Dynamic outdoor model with clean GPS data and diary	38	29.3	9.6	(20.0	27.9	38.7)
M8. Personal passive air sampler	10	24.2	6.1	(20.3	24.1	28.0)
<b>Third trimester</b>						
M1. Station-based static outdoor model	33	22.6	9.5	(16.6	18.0	27.8)
M2. Dispersion-based static outdoor model	33	27.9	8.3	(22.5	25.3	34.5)
M3. Dynamic outdoor model with raw GPS data	33	28.7	11.6	(19.8	28.5	35.3)
M4. Dynamic outdoor model with clean GPS data	33	27.0	8.5	(22.7	26.2	33.4)
M5. Dynamic outdoor model with clean GPS data and diary	33	27.8	8.4	(22.6	26.4	34.4)
M8. Personal passive air sampler	9	27.7	10.3	(20.5	23.5	31.3)
<b>Entire pregnancy</b>						
M1. Station-based static outdoor model	40	24.1	5.8	(19.7	23.7	28.9)
M2. Dispersion-based static outdoor model	40	29.0	4.5	(25.9	28.4	32.6)
M3. Dynamic outdoor model with raw GPS data	40	29.6	6.3	(25.5	28.9	33.1)
M4. Dynamic outdoor model with clean GPS data	40	27.7	4.8	(23.7	27.1	31.8)
M5. Dynamic outdoor model with clean GPS data and diary	40	28.9	4.6	(25.5	28.3	32.9)
M8. Personal passive air sampler	10	23.9	4.9	(20.5	23.4	26.6)

Models M6 and M7 are not mentioned as they are specific to PM<sub>2.5</sub> exposure.

Table 5

Spearman's rank correlation coefficients and Kappa estimates between the PM<sub>2.5</sub> exposure estimates from the various models.

Model and exposure window	N	M1			M2			M3			M4			M5			M6		
		r	p	K	r	p	K	r	p	K	r	p	K	r	p	K	r	p	K
<b>First trimester<sup>a</sup></b>																			
M1. Station-based static outdoor model	36	1.00																	
M2. Dispersion-based static outdoor model	36	0.97	<10 <sup>-4</sup>	0.92	1.00														
M3. Dynamic outdoor model with raw GPS data	36	0.85	<10 <sup>-4</sup>	0.58	0.87	<10 <sup>-4</sup>	0.58	1.00											
M4. Dynamic outdoor model with clean GPS data	36	0.93	<10 <sup>-4</sup>	0.75	0.94	<10 <sup>-4</sup>	0.67	0.89	<10 <sup>-4</sup>	0.75	1.00								
M5. Dynamic outdoor model with clean GPS data and diary	36	0.96	<10 <sup>-4</sup>	0.83	0.98	<10 <sup>-4</sup>	0.92	0.88	<10 <sup>-4</sup>	0.67	0.96	<10 <sup>-4</sup>	0.75	1.00					
<b>Second trimester</b>																			
M1. Station-based static outdoor model	38	1.00																	
M2. Dispersion-based static outdoor model	38	0.98	<10 <sup>-4</sup>	0.84	1.00														
M3. Dynamic outdoor model with raw GPS data	38	0.87	<10 <sup>-4</sup>	0.37	0.88	<10 <sup>-4</sup>	0.45	1.00											
M4. Dynamic outdoor model with clean GPS data	38	0.96	<10 <sup>-4</sup>	0.92	0.98	<10 <sup>-4</sup>	0.84	0.88	<10 <sup>-4</sup>	0.45	1.00								
M5. Dynamic outdoor model with clean GPS data and diary	38	0.98	<10 <sup>-4</sup>	0.84	0.99	<10 <sup>-4</sup>	0.92	0.88	<10 <sup>-4</sup>	0.53	0.99	<10 <sup>-4</sup>	0.92	1.00					
M6. Static indoor model	8	0.31	0.46	0.05	0.31	0.46	0.05	-0.21	0.61	0.05	0.31	0.46	0.05	0.31	0.46	0.05	1.00		
M7. Dynamic indoor and outdoor model	9	0.33	0.38	0.17	0.33	0.38	0.17	-0.08	0.83	0.00	0.25	0.52	0.17	0.33	0.38	0.17	1.00	<10 <sup>-4</sup>	1.00
<b>Third trimester</b>																			
M1. Station-based static outdoor model	33	1.00																	
M2. Dispersion-based static outdoor model	33	0.88	<10 <sup>-4</sup>	0.73	1.00														
M3. Dynamic outdoor model with raw GPS data	33	0.81	<10 <sup>-4</sup>	0.45	0.91	<10 <sup>-4</sup>	0.64	1.00											
M4. Dynamic outdoor model with clean GPS data	33	0.87	<10 <sup>-4</sup>	0.73	0.97	<10 <sup>-4</sup>	0.91	0.89	<10 <sup>-4</sup>	0.64	1.00								

Model and exposure window	N	M1			M2			M3			M4			M5			M6			
		r	p	K	r	p	K	r	p	K	r	p	K	r	p	K	r	p	K	
M5. Dynamic outdoor model with clean GPS data and diary	33	0.88	<10 <sup>-4</sup>	0.73	1.00	<10 <sup>-4</sup>	1.00	0.90	<10 <sup>-4</sup>	0.64	0.98	<10 <sup>-4</sup>	0.91	1.00						
M6. Static indoor model	9	-0.18	0.64	-0.33	0.03	0.93	-0.33	-0.08	0.83	0.00	-0.25	0.52	-0.17	-0.07	0.86	-0.33	1.00			
M7. Dynamic indoor and outdoor model	9	0.05	0.90	0.00	0.18	0.64	0.00	0.02	0.97	-0.33	-0.08	0.83	-0.17	0.12	0.77	0.00	0.87	<10 <sup>-4</sup>	0.67	
<b>Entire pregnancy<sup>b</sup></b>																				
M1. Station-based static outdoor model	40	1.00																		
M2. Dispersion-based static outdoor model	40	0.93	<10 <sup>-4</sup>	0.70	1.00															
M3. Dynamic outdoor model with raw GPS data	40	0.66	<10 <sup>-4</sup>	0.51	0.77	<10 <sup>-4</sup>	0.62	1.00												
M4. Dynamic outdoor model with clean GPS data	40	0.90	<10 <sup>-4</sup>	0.74	0.93	<10 <sup>-4</sup>	0.62	0.77	<10 <sup>-4</sup>	0.44	1.00									
M5. Dynamic outdoor model with clean GPS data and diary	40	0.90	<10 <sup>-4</sup>	0.66	0.97	<10 <sup>-4</sup>	0.70	0.80	<10 <sup>-4</sup>	0.51	0.96	<10 <sup>-4</sup>	0.77	1.00						
M6. Static indoor model	9	0.42	0.26	0.50	0.50	0.17	0.17	-0.03	0.93	0.00	0.33	0.38	0.17	0.55	0.12	0.50	1.00			
M7. Dynamic indoor and outdoor model	9	0.40	0.29	0.33	0.35	0.36	0.17	-0.10	0.80	0.00	0.25	0.52	0.17	0.47	0.21	0.33	0.85	<10 <sup>-4</sup>	0.33	

r: Spearman's rank correlation coefficient, p: p-value of Spearman's rank correlation coefficient, K: Kappa coefficient (based on PM<sub>2.5</sub> levels categorized in tertiles).

<sup>a</sup>: Indoor PM<sub>2.5</sub> measures were only performed in trimesters 2 and 3, not allowing to estimate models M6 and M7 for trimester 1.

<sup>b</sup>: Based on the average of entire pregnancy for models M1 to M5, and on the average of 2<sup>nd</sup> and 3<sup>rd</sup> trimesters for models M6 and M7.

Table 6

Spearman's rank correlation coefficients and Kappa estimates between the NO<sub>2</sub> exposure estimates from the various models.

Model and exposure window	N	M1			M2			M3			M4			M5		
		r	p	K	r	p	K	r	p	K	r	p	K	r	p	K
<b>First trimester</b>																
M1. Station-based static outdoor model	36	1.00														
M2. Dispersion-based static outdoor model	36	0.75	<10 <sup>-4</sup>	0.46	1.00											
M3. Dynamic outdoor model with raw GPS data	36	0.57	<10 <sup>-4</sup>	0.17	0.72	<10 <sup>-4</sup>	0.33	1.00								
M4. Dynamic outdoor model with clean GPS data	36	0.67	<10 <sup>-4</sup>	0.33	0.86	<10 <sup>-4</sup>	0.63	0.80	<10 <sup>-4</sup>	0.46	1.00					
M5. Dynamic outdoor model with clean GPS data and diary	36	0.71	<10 <sup>-4</sup>	0.38	0.96	<10 <sup>-4</sup>	0.67	0.75	<10 <sup>-4</sup>	0.42	0.90	<10 <sup>-4</sup>	0.58	1.00		
M8. Personal passive air sampler	8	0.50	0.21	0.24	0.52	0.18	0.24	0.24	0.57	0.05	0.45	0.26	0.24	0.43	0.29	0.43
<b>Second trimester</b>																
M1. Station-based static outdoor model	38	1.00														
M2. Dispersion-based static outdoor model	38	0.85	<10 <sup>-4</sup>	0.53	1.00											
M3. Dynamic outdoor model with raw GPS data	38	0.74	<10 <sup>-4</sup>	0.41	0.86	<10 <sup>-4</sup>	0.60	1.00								
M4. Dynamic outdoor model with clean GPS data	38	0.83	<10 <sup>-4</sup>	0.53	0.95	<10 <sup>-4</sup>	0.76	0.83	<10 <sup>-4</sup>	0.53	1.00					
M5. Dynamic outdoor model with clean GPS data and diary	38	0.86	<10 <sup>-4</sup>	0.53	0.98	<10 <sup>-4</sup>	0.84	0.87	<10 <sup>-4</sup>	0.53	0.96	<10 <sup>-4</sup>	0.84	1.00		
M8. Personal passive air sampler	10	-0.13	0.73	0.06	-0.13	0.73	0.09	-0.19	0.60	0.09	-0.36	0.31	-0.06	0.43	0.43	-0.06
<b>Third trimester</b>																
M1. Station-based static outdoor model	33	1.00														
M2. Dispersion-based static outdoor model	33	0.78	<10 <sup>-4</sup>	0.64	1.00											
M3. Dynamic outdoor model with raw GPS data	33	0.70	<10 <sup>-4</sup>	0.55	0.91	<10 <sup>-4</sup>	0.64	1.00								
M4. Dynamic outdoor model with clean GPS data	33	0.79	<10 <sup>-4</sup>	0.73	0.97	<10 <sup>-4</sup>	0.82	0.90	<10 <sup>-4</sup>	0.64	1.00					
M5. Dynamic outdoor model with clean GPS data and diary	33	0.76	<10 <sup>-4</sup>	0.64	0.99	<10 <sup>-4</sup>	1.00	0.93	<10 <sup>-4</sup>	0.64	0.98	<10 <sup>-4</sup>	0.82	1.00		
M8. Personal passive air sampler	9	0.30	0.43	0.17	0.12	0.77	0.17	-0.45	0.22	-0.17	-0.03	0.93	-0.33	0.22	0.58	0.17
<b>Entire pregnancy</b>																
M1. Station-based static outdoor model	40	1.00														
M2. Dispersion-based static outdoor model	40	0.67	<10 <sup>-4</sup>	0.32	1.00											
M3. Dynamic outdoor model with raw GPS data	40	0.54	<10 <sup>-4</sup>	0.29	0.83	<10 <sup>-4</sup>	0.59	1.00								

Model and exposure window	N	M1			M2			M3			M4			M5			
		r	p	K	r	p	K	r	p	K	r	p	K	r	p	K	
M4. Dynamic outdoor model with clean GPS data	40	0.66	<10 <sup>-4</sup>	0.36	0.94	<10 <sup>-4</sup>	0.70	<10 <sup>-4</sup>	0.90	<10 <sup>-4</sup>	0.62	1.00					
M5. Dynamic outdoor model with clean GPS data and diary	40	0.65	<10 <sup>-4</sup>	0.32	0.98	<10 <sup>-4</sup>	0.92	<10 <sup>-4</sup>	0.87	<10 <sup>-4</sup>	0.51	0.96	<10 <sup>-4</sup>	0.70	1.00		
M8. Personal passive air sampler	10	0.03	0.93	0.09	-0.16	0.65	-0.06	0.40	-0.30	0.40	-0.36	-0.42	0.23	-0.06	-0.39	0.26	-0.21

r: Spearman's rank correlation coefficient, p: p-value of Spearman's rank correlation coefficient, K: Kappa coefficient (based on NO<sub>2</sub> levels categorized in tertiles).

Models M6 and M7 are not mentioned as they are specific to PM<sub>2.5</sub> exposure.